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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SRIVASTAVA, KAILASH C	

ART UNIT	PAPER NUMBER
1657	

NOTIFICATION DATE	DELIVERY MODE
02/17/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/583,275	HONDA ET AL.	
	Examiner	Art Unit	
	Kailash C. Srivastava	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 September 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *27-51* is/are pending in the application.

4a) Of the above claim(s) *34-42 and 46-51* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27-33 and 43-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 July 2007* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *06/16/2006 & 03/14/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Notice to Comply*

DETAILED ACTION

1. Amendment and response filed 29 September 2010 to Office Action with election/restriction requirement mailed 09 August 2010 is acknowledged and entered.

Claims Status

2. According to the amendment filed 29 September 2010, following is the current Claims status:

- ☒ Claims 1-26 have currently been cancelled;
- ☒ Claims 27-51 have currently been added;
- ☒ Claims 27-51 are presented for examination.

Restriction/Election

3. Election without traverse of Group I invention encompassing original Claims 1-5, 7-8 and 18-20, corresponding to newly presented Claims 27-33 and 43-45 filed 29 September 2010 to Office Action with election/restriction requirement mailed 09 August 2010 is acknowledged and entered. Since the election is made without traverse, the restriction requirement is deemed proper and is made FINAL.

4. Accordingly, Claims 34-42 and 46-51 are withdrawn from further consideration as being directed to a non-elected invention. See 37 C.F.R. §1.142(b) and M.P.E.P. § 821.03.

5. Claims 27-33 and 43-45 are examined on merits as invention of Group I.

Priority

6. Claim for foreign priority under 35 U.S.C. §119 (a-d) to PCT/JP04/18895/ filed 17 December 2004 is acknowledged.

Information Disclosure Statement

7. The Information Disclosure Statements (i.e., IDSs) filed respectively on 16 June 2006 and on 14 March 2008 are acknowledged, have been made of record, considered and duly

initialed USPTO forms, a total of 2 sheets are enclosed with the instant Office Action

Specification Objected

8. The specification is objected to because Line one of first page of specification, in its present form does not properly recite the application priority data. Please perfect the application priority data.

9. Specification is also objected because the structure of cresyl violet as currently presented in the specification is not consistent with that known in the art (see e.g., Structure obtained in the NPL search).

Sequence Compliance/Specification Objected

10. Instant application contains sequence disclosure noticed e.g., at page 10, lines 13-15 and 22-25; page 11, lines 3 and 6, that is encompassed by the definitions for nucleic acid/amino acid sequences set forth in 37 C.F.R. §1.821(a) (1) and (a) (2). However, the instant application fails to comply with the requirements of 37 C.F.R. §1.821 through §1.825 To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. See attached Notice to Comply. Appropriate correction is required.

The disclosure is objected to because of the following informalities:

The Brief Description of Figures 11 and 12 does not make sense.

Appropriate correction is required.

Claims Objected

11. Claims 43-44 as currently presented are objected to for following reasons:

- Each of Claims 43-33 describe that the amino group, amino acid, or oligopeptide (Claim 43 only) is bound to one or more of said at least one amino group through an amide

bond. It is not clear whether the colored moiety/pigment is attached to the peptide/amino acid with an amide bond, or the amino group of the amino acid/or peptide to another amino acid or peptide. If protease activity needs to be determined, more than likely the pigment/chromogen/fluorogen would be linked to the amino acid/peptide/oligopeptide with an amide bond/linkage.

Appropriate correction /clarification is in order.

Claim Rejections - 35 U.S.C. §112
First Paragraph Rejections

12. The following is a quotation of the first paragraph of 35 U.S.C. §112:

> **The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.**

13. Claims 27-33 and 43-45 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with those claims.

The claims are drawn to a method to measure an allergen by measuring the protease activity of said allergen when a test material having said allergens is brought in contact with a protease substrate, **without a pretreatment to said test material.**

From the record of the present disclosure, however, the specification according to the currently presented description does not enable an artisan of skill to practice the invention as claimed for the following reasons:

- the claimed invention in absence of a clear and succinctly evidenced method supported with clear data to evidence that the protease activity of an allergen containing test material was determined without pretreating said test material.

- absence of demonstrated evidence of record that said method comprising no pretreatment of test sample prior to subjecting said material for the protease activity assay.

Thus, specification as currently presented while enabling to assay protease activity in an allergen comprising a sample by subjecting said sample to different steps until said sample or a material obtained from said sample is applicable for assaying protease activity by bring in contact a protease substrate with said material obtained from said test-sample. Therefore, as currently presented, the specification does not provide for one of ordinary skill to practice the invention as claimed.

A person of ordinary skill would be unable to practice the invention as claimed, because undue experimentation will be required to obtain a method to determine protease activity of an allergen comprising test material without any type of pre-treatment of said allergen comprising test material as currently presented in the specification due to the quantity of experimentation necessary; limited amount of guidance and limited number of working examples in the specification; nature of the invention; state of the prior art; relative skill level of those in the art; predictability or unpredictability in the art; and breadth of the claims. In re Wands, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) as illustrated infra.

a. Quantity of Necessary Experimentation

The phrase, pre-treatment is broadly interpreted as any manipulation/ maneuvering of the sample prior to said sample being actually tested. The steps described in the specification prior to taking 40 μL aliquots of the material that was first suspended in phosphate buffer and subsequently incubated at 37 °C for 10 minutes (See, bellow) is broadly interpreted as pre-treatment because the sample has been maneuvered before actual steps of assaying the protease activity. The actual steps of encompassing as adding the substrate to the sample (i.e., source of enzyme).

The description given in the specification as currently presented, however, does not provide the evidence that an allergen comprising test sample was directly tested without any pretreatment given to said sample (See, e.g., Example 1, Lines 7-12). At said citation, the description in the specification describes that frozen mite samples were first suspended in aqueous phosphate buffer followed by addition of 20μL of 100 mM L-cysteine solution to each 180 μL mite suspension in aqueous phosphate buffer and subsequently incubating said mixture at 37 °C for 10 minutes. A 40 μL aliquot of said mixture was added to 10μL of protease substrate to

determine the protease activity (Page 21, lines 12-17). In Example 2 also there are pre steps described (Page 22, Lines 6-9) prior to actual assay of test sample for protease activity (Page 22, Lines 10-13).

b. Limited Amount of Guidance

As illustrated in item "a" supra, the specification as currently presented does not provide a clear-cut guidance to obtain the claimed invention of a method to measure biological allergen in a test sample without pre-treating said test sample. Thus, in a preferred mode of the present invention, the environmental biological allergen(s) is (are) subjected to the measurement as it (they) is (are) or after merely being dissolved or suspended in water or in a buffer, without any pretreatment such as extraction or purification, so that the method is extremely simple.

c. Limited Number of Working Examples in the Specification

The specification or the claims as currently presented do not clearly define all the embodiments. Any evidence, if provided in the specification is unsubstantiated with a method to measure the protease activity, wherein a protease substrate is directly added to the test-sample and the protease activity is measured in an aqueous suspension of said test sample.

d. Nature of the Invention

From the facts discussed in items "a" and "c" supra, the instantly claimed invention is unclearly defined and is not concise and clear.

e. State of the Prior Art

The discussion on the prior art as currently presented in the specification is adequate and succinct description of the prior art.

f. Relative Skill Level of those in the Art

At least a Bachelor Degree in Biochemical engineering, Biochemistry, Biology, Biomedical engineering, Biophysics, Chemical engineering, Chemistry, Environmental science and engineering, Material science and engineering, Clinical Medicine, Microbiology, Molecular biology, Pharmaceutical Sciences, or Pharmacology.

g. Predictability or Unpredictability in the Art

Unless supported with illustrative experimental evidence, biological responses are

unpredictable. Thus, information obtained under one set of detrimental parameters may not be extrapolated for another set of parameters/environmental or specific conditions.

h. Breadth of the Claims

The claimed invention is drawn upon claims that are not supported by the presently detailed specification.

Claim Rejections - 35 U.S.C. §102

14. The following is a quotation of 35 U.S.C. §102(b) which forms the basis for all obviousness rejections set forth in this Office action:

> **A person shall be entitled to a patent unless –**
>
> **(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.**

15. Claims 27-28, 30 and 32-33 are rejected under 35 U.S.C. § 102(b) as anticipated by Pirzad (GB 2351560 A1, Item BA, Applicants' IDS filed 03/14/2008).

In Claims 27-28, 30 and 32-33 is recited a method to measure environmental biological allergens in a sample by measuring the protease activity of said samples comprising:

- contacting a protease substrate with said test sample, without pre-treating said sample (Claim 27;
- said allergens are mite, or a material originating from mite and/or pollen (Claim 28);
- said sample is obtained from room air, floor, walls, windows including frame, floor coverings, bedding, furniture, dust (Claim 30); and
- said enzyme substrate is on a porous support (Claims 32-33);

The invention claimed in instant Claims 27-28, 30 and 32-33 given broadest possible interpretation is interpreted as an assay method to assay protease with the addition of a chromogenic substrate.

Pirzad teaches (See Claims 16) a method to determine allergen activity in dust (i.e., limitation in Claims 27-28 and 30) comprising the steps of:

- providing a dust sample;
- protease substrate having a matrix (Page 3, Lines 15-20) that comprises a filter (Page 5, Line 11, i.e., limitations of Claims 32-33), said substrate has immobilized on it proteins or peptides (Page 3, Lines 16-17; Claim 16, Lines 4-5) said peptides or proteins labeled with a chromogenic material, i.e., 1,4,6-trinitrobenzene sulphonic acid-TNBSA, Page 5, Lines 19-20 & Claim 16, Line 6);
- when protease substrate is exposed to said dust sample allowing the protease in said dust sample to react with said provided substrate to produce mobile chromogen labeled components (Claim 16);
- quantitatively measuring said coloration (Claim16, Line 12); and
- comparing the color developed with a comparative color chart to indicate the intensity of color, wherein color intensity is directly proportional to the allergen quantity (Claim 16, Lines 13-14).

Thus, Pirzad teaches (See, Figure 4 in combination with Figure 1) placing a dust sample in contact with a protease substrate l (imitations in Claims 27-28 and 30), said protease substrate is comprised of a porous matrix support and because said matrix is comprised of a filter and on said substrate support a chromogen-labeled peptide or protein is immobilized (limitations of Claims 32-33). Furthermore, upon reaction of protease in the sample with said support comprising chromogen labeled protease substrate, the chromogenic material is released. The color intensity of said chromogenic material is directly proportional to the allergen quantity.

Therefore, the reference is deemed to anticipate the recited Claims 27-28, 30 and 32-33.

Claim Rejections - 35 U.S.C. §103

16. The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> **(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.**

17. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. §1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. § 103(c) and potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103(a).

18. Claims 29 and 43-44 are rejected under 35 U.S.C. §103(a) as obvious over combined teachings from Pirzad (GB 2351560 A1, Item BA, Applicants' IDS filed 03/14/2008) in view of Berrens (U.S. Patent 5,667,979A, Item AA, Applicants' IDS filed 16 June 2006).

In Claims 29 and 43-44 is recited a method to measure environmental biological allergens in a sample by measuring the protease activity of said samples wherein:

- allergen are, or originates from cedar pollen (Claim 29); and
- substrate is a colored pigment compound bound to an amino acid, peptide or oligopeptide with an amide bond (Claims 43-44).

The invention claimed in instant Claims 29 and 43-44 given broadest possible interpretation is interpreted as an assay method to assay protease with the addition of a chromogenic protease substrate, wherein as required in Claim 31 the enzyme activity is measured as function of "change in absorption as a result of enzyme reaction". The absorption is also measured as optical density".

Teachings from Pirzad (2001) have been discussed supra. Pirzad, however, is silent to measure protease activity in the reaction mixture comprising protease substrate and the pollen/allergen/cedar pollen preparations.

Berrens teaches:

- a chromogenic protease substrate, H-D-Isoleucyl-L-prolyl-L-arginine-p-nitroanalide-di HCl, (i.e., IPA, Column 7, Lines 45-47, limitations in Claims 43-44);

- assaying protease activities (expressed as VLA mud/mg in Table D) of pollen preparations from Junipers monospermous (i.e., cedar) by measuring optical density change to a reaction mixture comprising: 15 μL of 1.5 μMole/mol) synthetic protease substrate H-D-Valyl-Leucyl-Lysine-p-nitroanilide, 2 HCl (i.e., VLL) 200 μL samples of pollen preparations dissolved in 200 μL TRIS-HCl buffer (0.05M pH 8.3, containing 0.01% w/v Tween-20) into microtiter plate flat-bottom wells. The plates covered with Para film and kept at 37 °C for 2.5 hours. The reaction was then stopped by adding 25 μL 50% acetic acid and the optical density was evaluated at 410 nm in an ELISA-Reader (Column 13, Lines 37-49).

Thus, as illustrated supra, Berrens teaches assaying protease enzyme activity in cedar pollen preparations (Column 13, Lines 37-49, Table D; Limitations in Claims 29) by adding a protease substrate comprising peptides bound to a colored compound (i.e., chromogen, Limitations in Claims 43-44)) and further measuring the change in optical density of the reaction mixture in comparison with a control (Column 9, Lines 51-53). That is each of the limitations in each of Claims 29 and 43-44 to assay the protease activity. in samples comprising cedar pollens.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made and one having ordinary skill in the art at the time of the claimed invention would have been motivated to modify/combine the teachings from Pirzad by substituting Berrens' teachings' to obtain a method to assay protease activities from the samples comprising allergens in pollens and or dust mites from environmental samples by adding a substrate having a chromogen bound to a peptide and evaluating the optical density of the reaction mixtures**; because** Berrens teaches assaying protease activity in dust mite/pollen samples with a substrate comprising a peptide bound to a chromogen and measuring the allergenic/protease activity as a function of change in absorbance (i.e., O.D.) with appropriate controls. A person of ordinary skill would have been able to substitute the peptides bound to a support as Pirzad teaches with Berrens' protease substrate.

From the teachings of the references cited supra, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

19. Claims 28 and 31 are rejected under 35 U.S.C. § 103 (a) as obvious over combined teachings from Pirzad (GB 2351560 A1, Item BA, Applicants' IDS filed 03/14/2008) in view of Berrens (U.S. Patent 5,667979A, Item AA, Applicants' IDS filed 16 June 2006) as applied to Claims 29 and 43-44 above and further in view of Ino et al., (1989. Characterization of the Proteases in the Crude Mite Extract. International Archives of Allergy and Applied Immunology, Volume 89, Pages321-326).

In Claims 28 and 31 are described additional limitations:

- "allergen is mite and/or a material originated from mite" (Claim 28); and
- "substrate of the enzyme used for the measurement of the enzyme activity brings about fluorescence emission as a result of enzyme reaction" (Claim 31).

Ino et al., teach a method to measure the protease activity in mite preparations according to the following steps:

- 1 Gram defatted mites suspended in phosphate buffered saline (i.e., 2 mM phosphate buffer comprising 85 mM NaCl, pH7.4), mixture rotated/stirred for 48 hrs at 4 °C, subsequently filtering and lyophilizing the filtrate (Page 321, Column 2, Lines 29-37; Limitation in Claim 28));

- A reaction mixture comprising: 0.1 mL mite preparation, and 0.9 ml of a protease substrate (e.g., t-Butyloxycarbonyl-L-phenylalanyl-L-seryl L-arginine 4-methyl-coumaryl-7-amide (i.e., Boc-Phe-Ser-Arg-MCA) at 10 μmol concentration in 100 mM phosphate buffer incubated at 37 °C for 15 min, 2 mL of 15% acetic acid added

to said mixture and the fluorescence of aminomethylcoumarin released in the reaction mixture measured at 380 nm and emission 460 nm on a fluorometer. (Page 322, Column 1, Lines 1-16 under Figure 1; Limitations in Claims 27-31); and

- Expressing the protease activity of the preparation as enzyme activity in nmol/mL/min., (See, e.g., Figure 2).

Thus, as illustrated supra, Ino et al., teach the additional limitations in each of Claims 28 and 31 because the mite preparation prepared from frozen mite samples comprise materials from mites (limitation in Claim 28). Additionally, the protease activity is assayed by measuring the fluorescence from the reaction mixture post enzyme catalysis, wherein enzyme (i.e., protease) is present in the mite sample and the substrate for said enzyme is a peptide bound to a fluorogen (i.e., Boc-Phe-Ser-Arg-MCA). Thus, as per the requirements of Claim 28, Ino et al., teach materials originated from mite and protease activity is measured by fluorescence emission from the product formed post enzyme reaction (i.e., limitation in Claim 31).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made and one having ordinary skill in the art at the time of the claimed invention would have been motivated to modify/combine the teachings from Pirzad by substituting Berrens' teachings and according to the teachings from Ino et al., to obtain a method to assay protease activities from the samples comprising allergens in pollens and or dust mites from environmental samples by adding a substrate having a chromogen/fluorogen bound to a peptide and evaluating the absorption/optical density/fluorescence of the reaction mixtures**; because** Berrens teaches assaying protease activity in dust mite/pollen samples with a substrate comprising a peptide bound to a chromogen and measuring the allergenic/protease activity as a function of change in absorbance (i.e., O.D.) with appropriate controls. A person of ordinary skill would have been able to substitute the peptides bound to a support as Pirzad teaches with Berrens' protease substrate and Ino et al., teach assaying protease activity in a sample comprising allergens in materials originating from mite by measuring the fluorescence of the reaction mixture post enzyme reaction.

From the teachings of the references cited supra, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

20. Claim 45 is rejected under 35 U.S.C. § 103 (a) as obvious over combined teachings from Pirzad (GB 2351560 A1, Item BA, Applicants' IDS filed 03/14/2008) in view of Berrens (U.S. Patent 5,667979A, Item AA, Applicants' IDS filed 16 June 2006) as applied to Claims 29 and 43-44 above and further in view of Bissell et al (U. S. Patent 6,235,493 B1).

In Claim 45 is described additional limitation:

- "the pigment attached to the amino group of amino acid, peptides or oligoppeptide is cresyl violet, Safranin O, or methylene violet 3RAX".

Bissell et al., teach:

- amino acid substituted-cresyl violet a fluorogenic substrate for the analysis of agents in tissue (title);

- teach a method to assay an enzyme present in a tissue or cell sample, whereby said enzyme cleaves the cresyl violet and cleaved cresyl violet is released in the sample thereby producing a color/ fluorescence change in the sample (Abstract, Lines 22-25);

- said fluorescence can be quantified and compared with a pre-calibrated fluorescence scale (abstract items d-e).

Thus, as illustrated supra, Bissell et al., teach the additional limitations in Claim 45 of a pigment\ bound to an amino acid and further teach that when an enzyme present in a cell or tissue sample is contacted with said material the cresyl violet cleaves in to the reaction mixture, produces color change which is the manifestation of fluorescence because the mites preparation prepared from frozen mite samples comprise materials from mites Additionally, the protease activity is assayed by measuring the fluorescence from the

reaction mixture post enzyme catalysis, wherein enzyme (i.e., protease) is present in the mite sample and the substrate for said enzyme is a peptide bound to a fluorogen (i.e., Boc-Phe-Ser-Arg-MCA).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made and one having ordinary skill in the art at the time of the claimed invention would have been motivated to modify/combine the teachings from Pirzad by substituting Berrens' teachings and according to the teachings from Bissell to obtain a method to assay protease activities from the samples comprising allergens in pollens and or dust mites from environmental samples by adding a substrate having a chromogen/fluorogen bound to a peptide and evaluating the absorption/optical density/fluorescence of the reaction mixtures**; because** Berrens teaches assaying protease activity in dust mite/pollen samples with a substrate comprising a peptide bound to a chromogen and measuring the allergenic/protease activity as a function of change in absorbance (i.e., O.D.) with appropriate controls. And Bissell teaches a cromogen (i.e., cresyl violet) attached to a an amino acid/peptide A person of ordinary skill would have been able to substitute the peptides bound to a support as Pirzad teaches with Berrens' protease substrate and Bissell's chromogenic peptide to assay the protease activity in a sample comprising allergens in materials originating from mite/pollens by measuring the fluorescence of the reaction mixture post enzyme reaction/catalysis.

From the teachings of the references cited supra, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

21. For reasons aforementioned, no Claims are allowed.

22. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Kailash C. Srivastava whose telephone number is (571) 272-0923.

The examiner can normally be reached on Monday to Thursday from 7:00 A.M. to 5:30 P.M. (Eastern Standard or Daylight Savings Time).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Jon Weber, can be reached on (571)-272-0025 Monday through Thursday 7:30 A.M. to 6:00 P.M. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding may be obtained from the Patent Application Information Retrieval (i.e., PAIR) system. Status information for the published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (i.e., EBC) at: (866)-217-9197 (toll-free). Alternatively, status inquiries should be directed to the receptionist whose telephone number is (703) 308-0196.

/Kailash C Srivastava/
Examiner, Art Unit 1657
(571) 272-0923

/JON P WEBER/
Supervisory Patent Examiner, Art Unit 1657